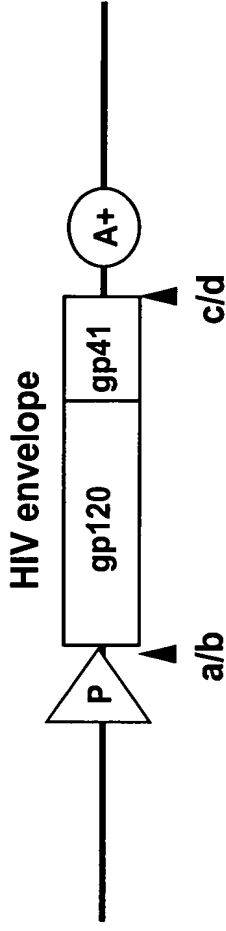


PhenoSense HIV Entry Assay

Envelope Expression Vector: pHIVenv



HIV-1 Expression Vector: pHIVluc Δ U3

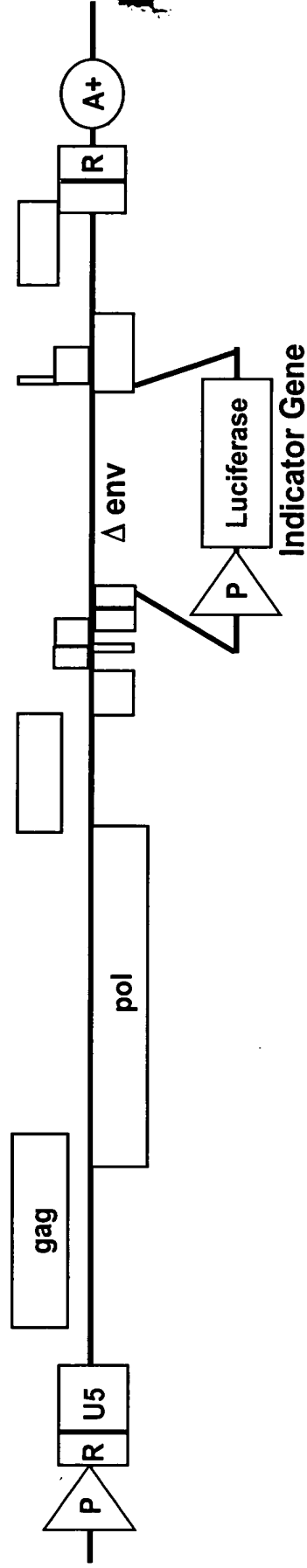


Fig. 1A



PhenoSense™ HIV: Cell Assay

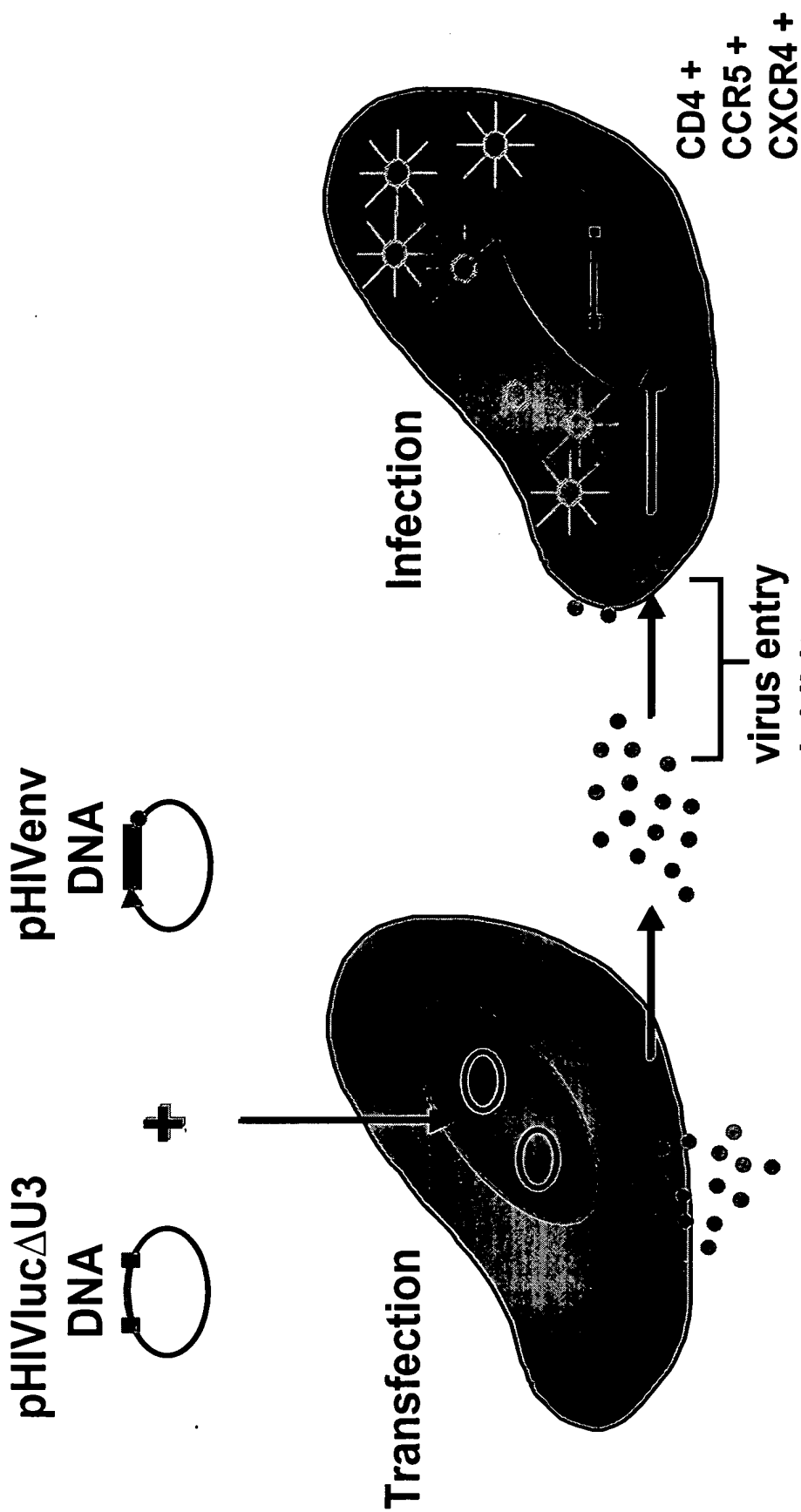


Fig. 1B

HIV Envelope Expression Strategies

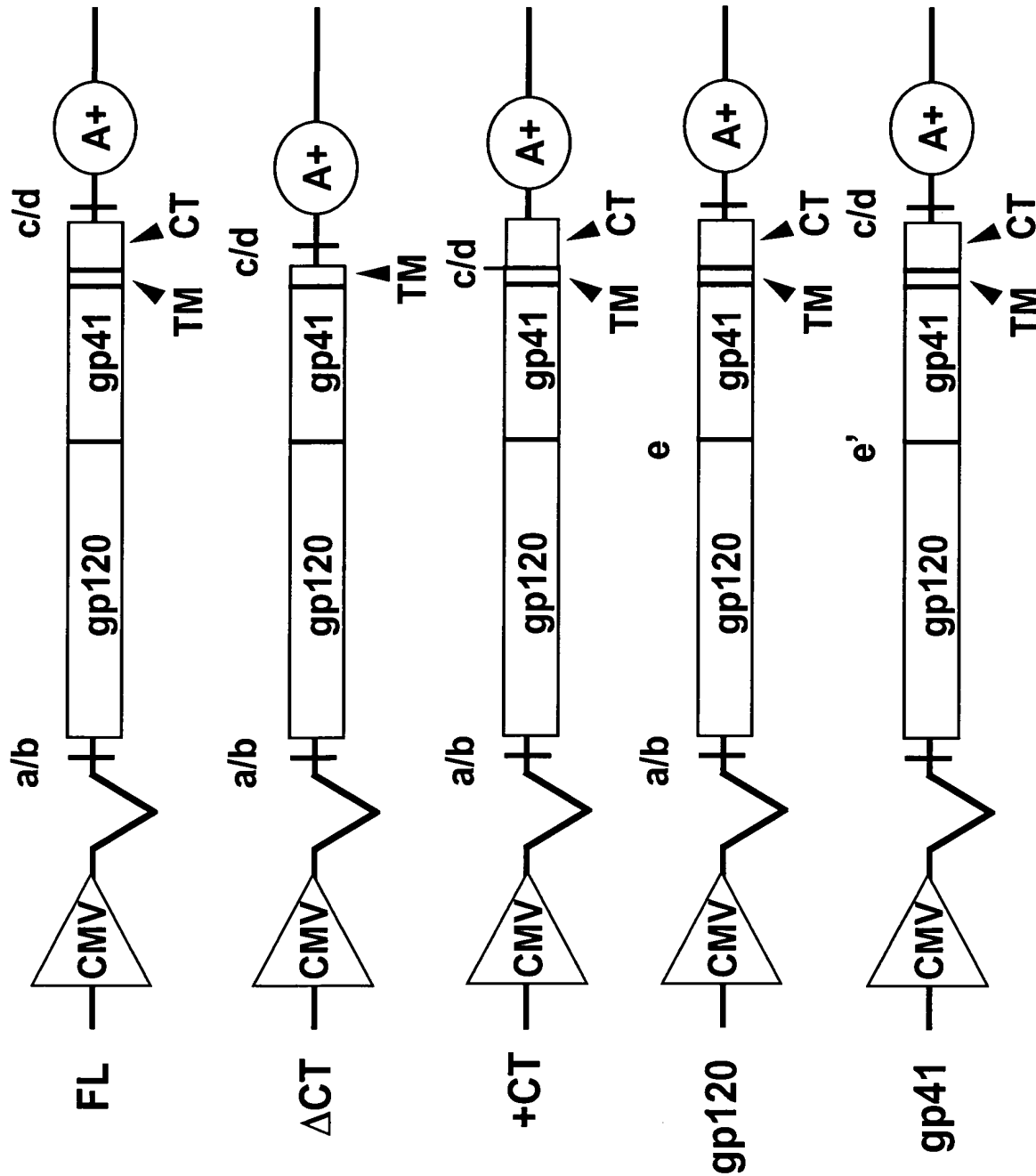
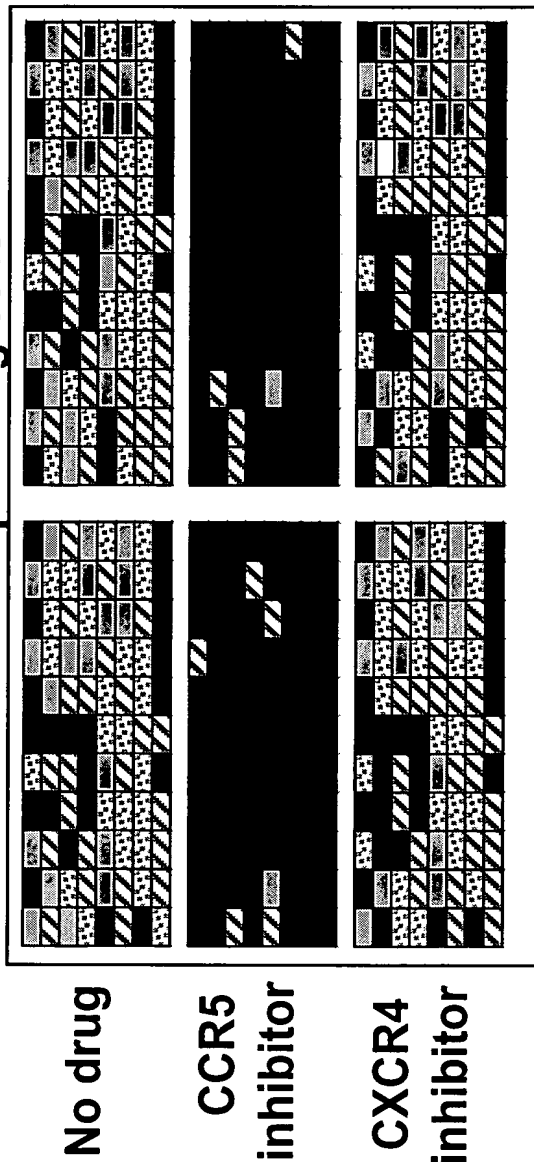


Fig. 2

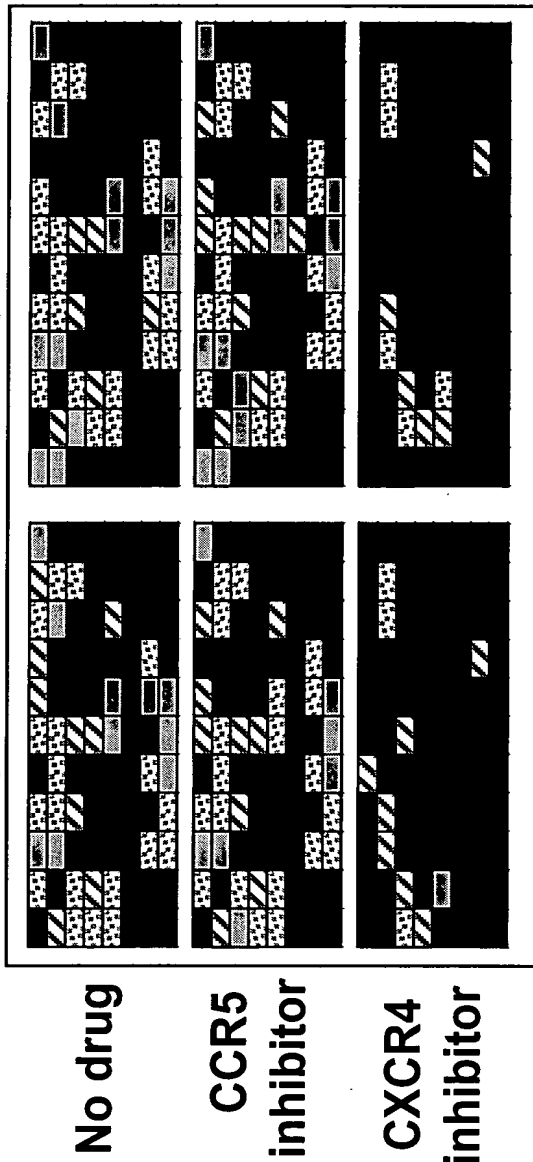
Co-Receptor Tropism Screen

CCR5-expressing cells



Replicate 1

Replicate 2



CXCR4-expressing cells

Fig. 3A

<100 RLU

100-1000 RLU

1000-10,000 RLU

>10,000 RLU

Co-Receptor Tropism Assay Interpretation

3

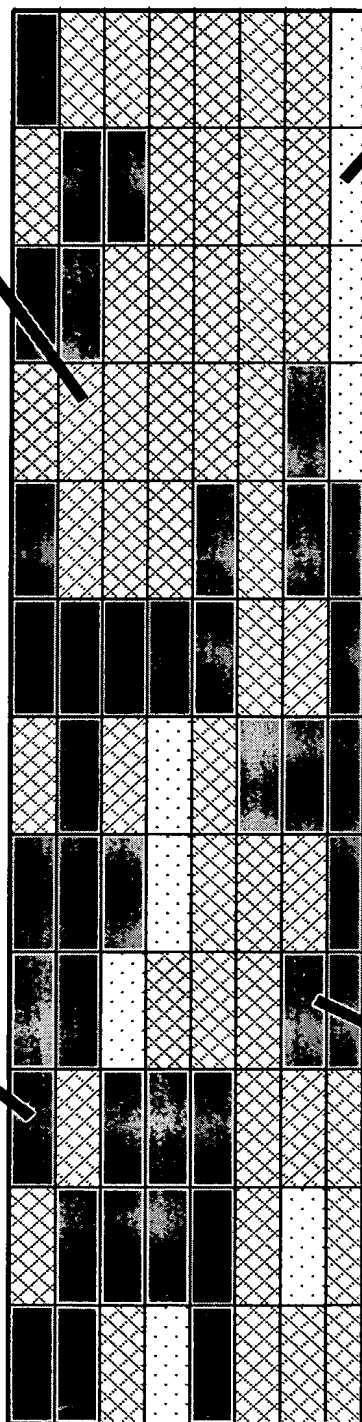
| R5 cells | X4 cells | R5:X4 |
|----------|----------|-------|
| 34 | 26,471 | 0 |
| | 19,258 | |
| | 32 | |
| | 27 | |
| | 100 | |

no drug
R5 inhibitor
X4 inhibitor
%inhib by R5 inhibitor
%inhib by X4 inhibitor

21

| R5 | X4 | R5:X4 |
|--------|----|-------|
| 67,389 | 72 | 936 |
| 99 | | |
| 42,295 | | |
| 100 | | |
| 37 | | |

no drug
R5 inhibitor
X4 inhibitor
%inhib by R5 inhibitor
%inhib by X4 inhibitor



| |
|---------------|
| CXCR4 |
| CCR5 |
| DUAL or MIXED |
| NON-VIABLE |

active RLU limit: 100
tropism ratio limit: 5

76

| R5 | X4 | R5:X4 |
|--------|--------|-------|
| 14,982 | 12,020 | 1 |
| 111 | 10,839 | |
| 8,580 | 3,384 | |
| 99 | 10 | |
| 43 | 72 | |

no drug
R5 inhibitor
X4 inhibitor
%inhib by R5 inhibitor
%inhib by X4 inhibitor

95

| R5 | X4 | R5:X4 |
|----|----|-------|
| 43 | 42 | |
| | | |
| | | |
| | | |
| | | |

no drug
R5 inhibitor
X4 inhibitor
%inhib by R5 inhibitor
%inhib by X4 inhibitor

Fig. 3B



Entry Inhibitor Susceptibility: Fusion Inhibitor

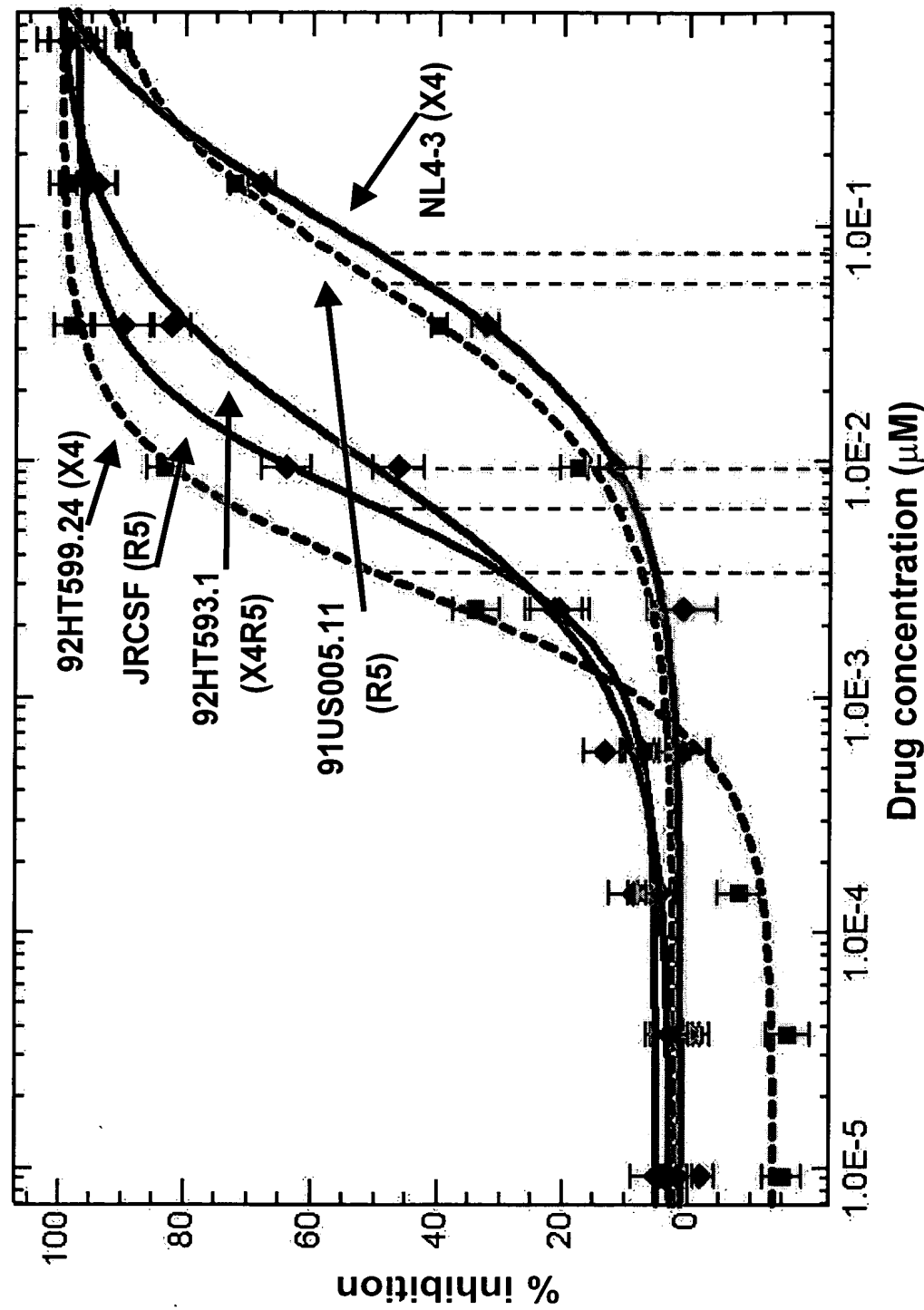


Fig. 4A

Reduced Susceptibility: Fusion Inhibitor

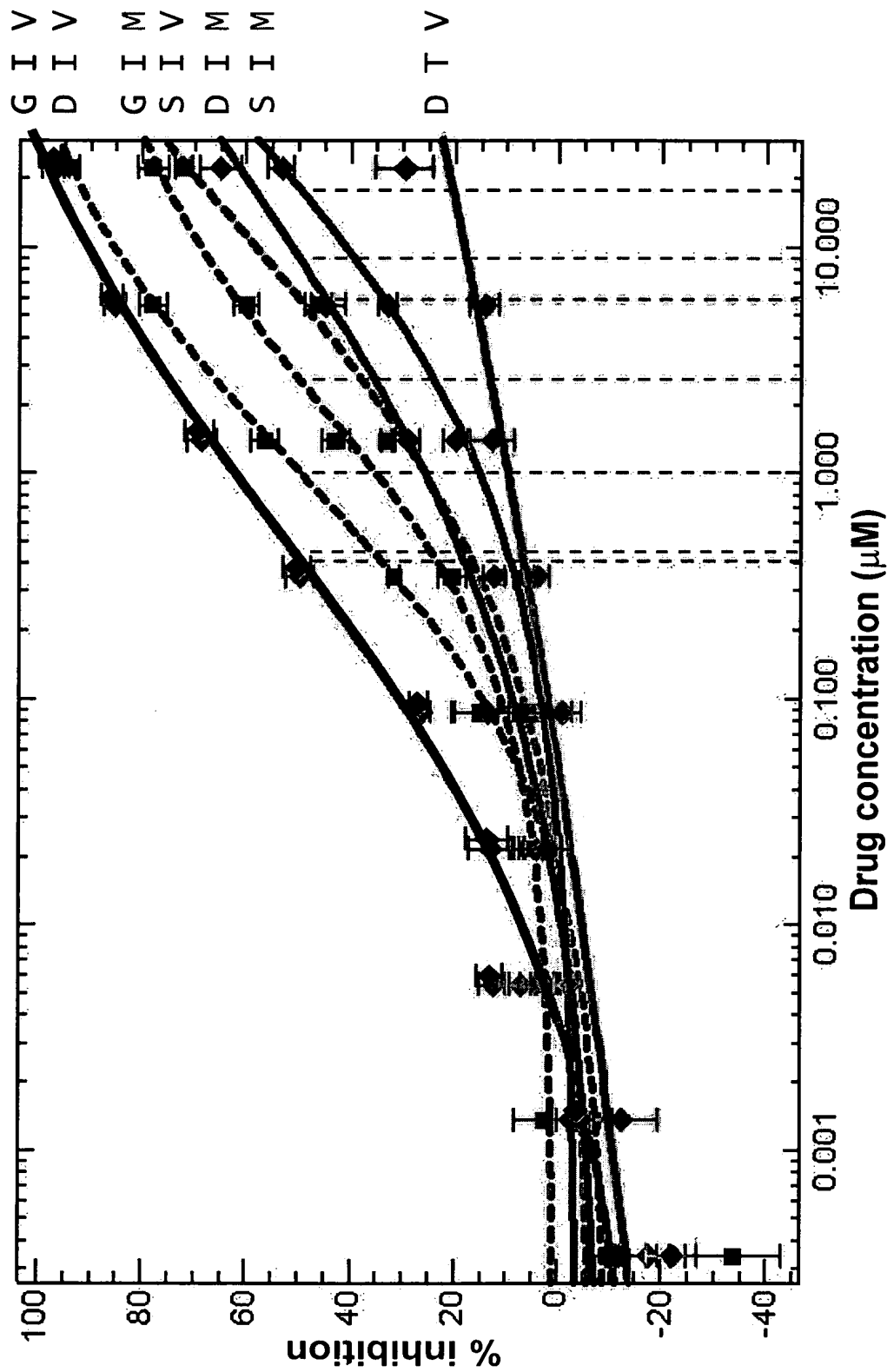


Fig. 4B



Entry Inhibitor Susceptibility: CCR5 Inhibitor

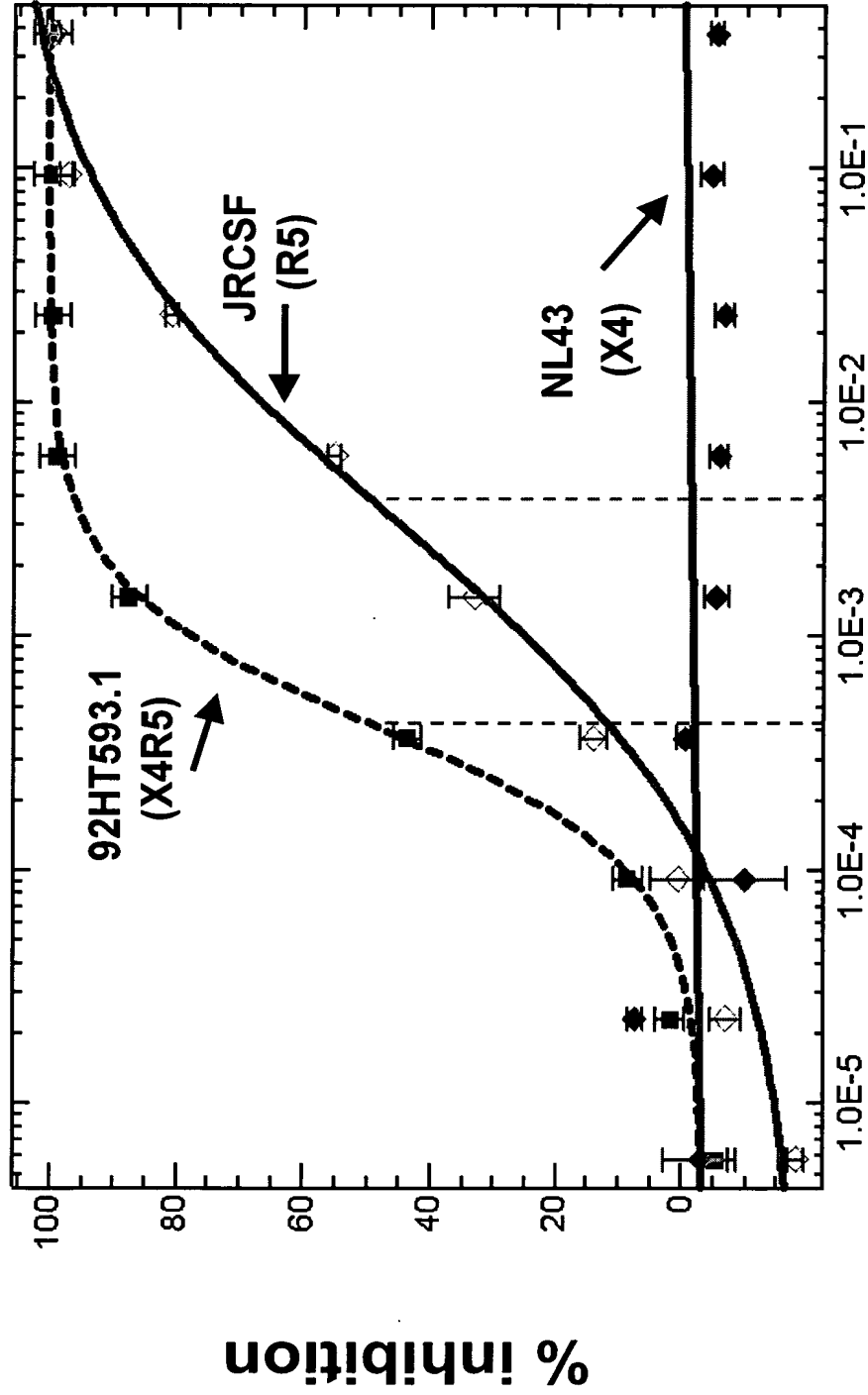


Fig. 5A

Drug: R5 Inhibitor
Cell: CD4/CCR5



Entry Inhibitor Susceptibility: CXCR4 Inhibitor

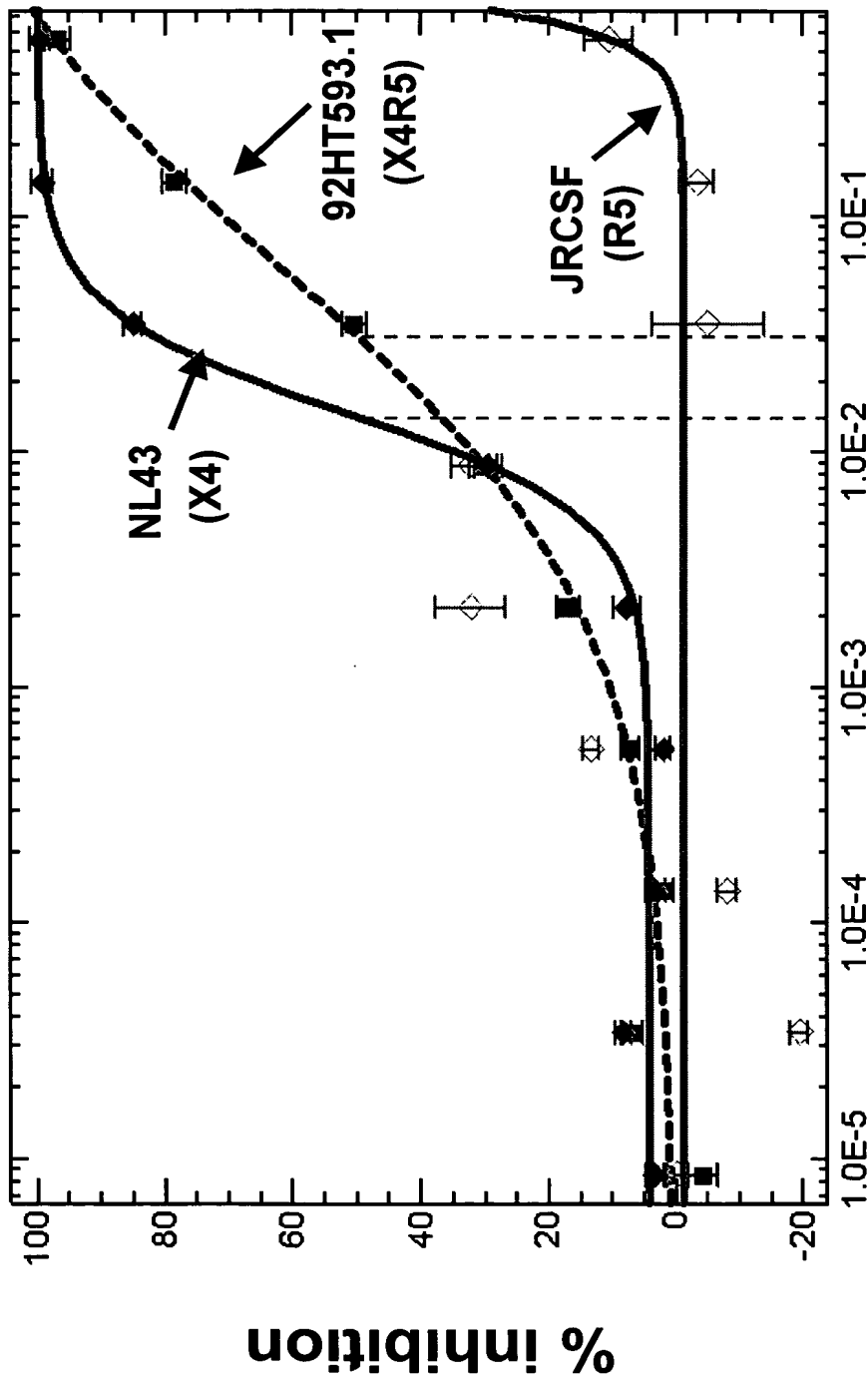
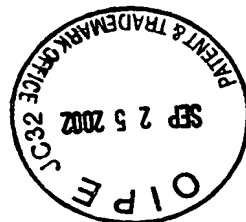
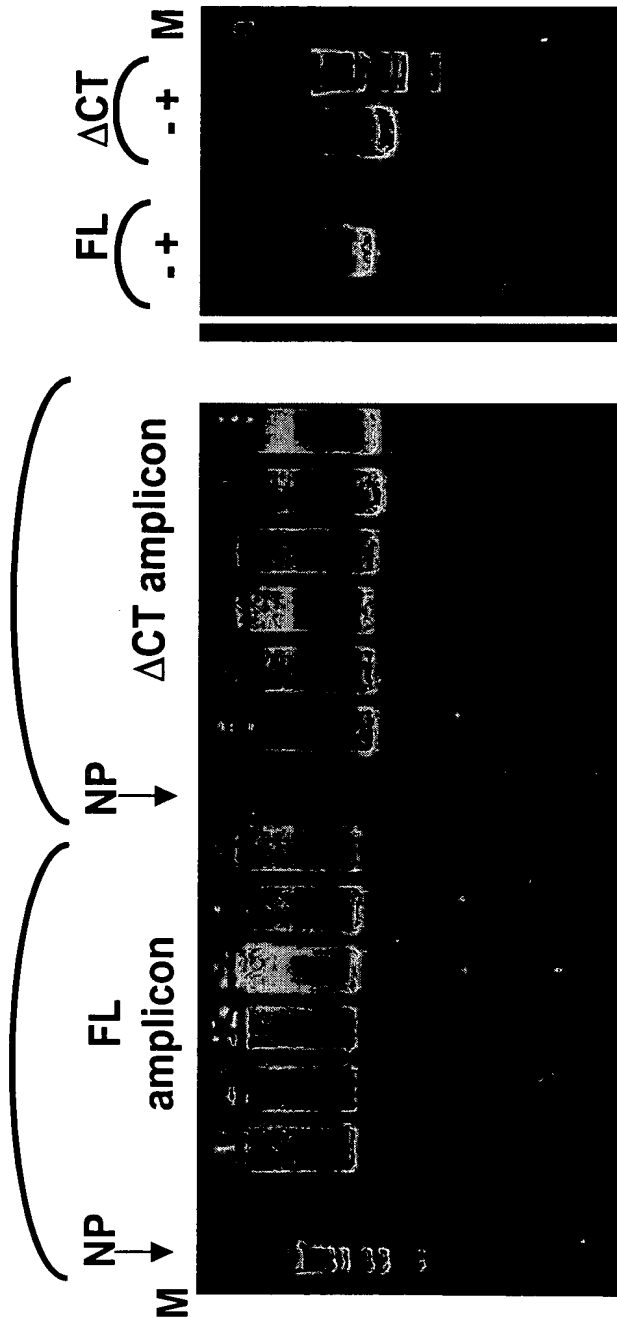


Fig. 5B

Drug: X4 Inhibitor
Cell: CD4/CXCR4



Envelope Sequence Amplification

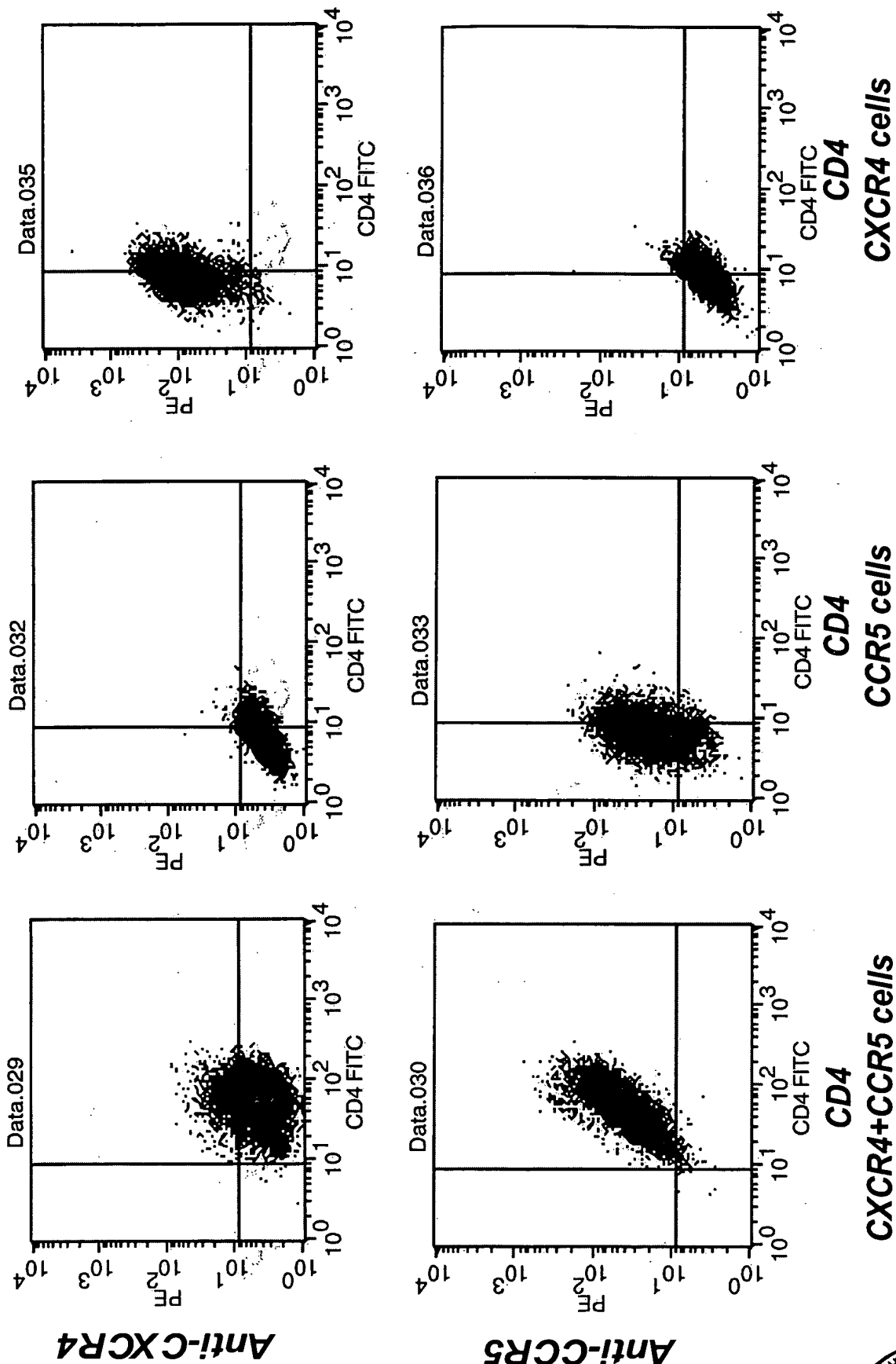


| <u>Co-Receptor Tropism</u> | | | | | | <u># of isolates</u> | |
|----------------------------|---|---|---|---|---|----------------------|--|
| 1 | 2 | 3 | 4 | 5 | 6 | 15 | |
| X4 | | | | | | 24 | |
| R5 | | | | | | 15 | |
| X4/R5 | | | | | | 35 | |
| Undefined | | | | | | | |
| <u>Envelope Subtype</u> | | | | | | <u># of isolate</u> | |
| Clade A | | | | | | 2 | |
| Clade B | | | | | | 76 | |
| Clade C | | | | | | 7 | |
| Clade D | | | | | | 1 | |
| Clade E | | | | | | 3 | |

Fig. 6

Target Cell Receptor and Co-Receptor Expression

Fig. 7



Inhibition By Co-Receptor Antagonists

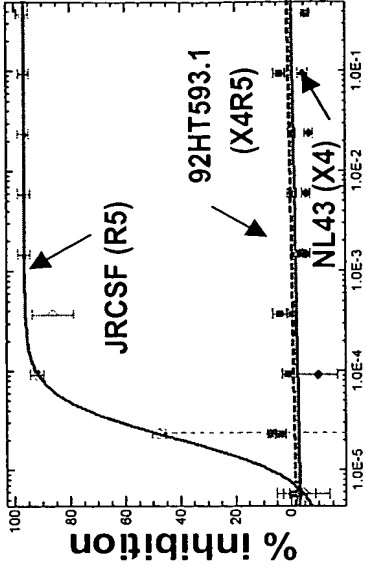
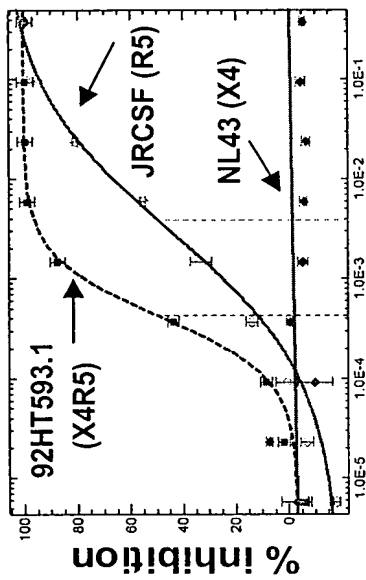
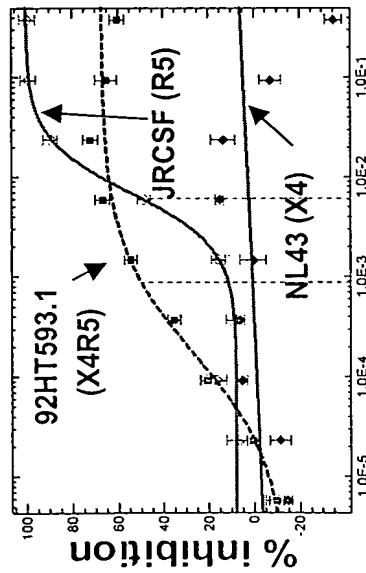
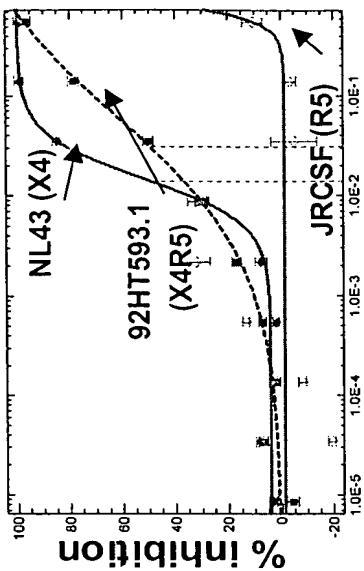
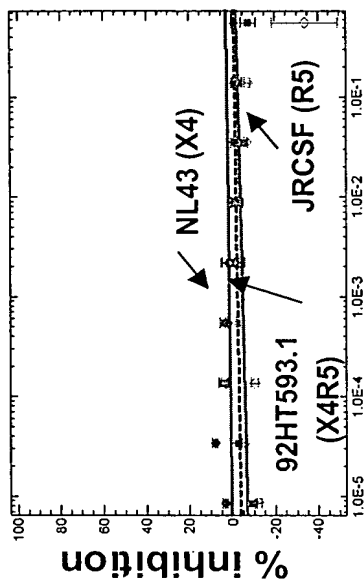
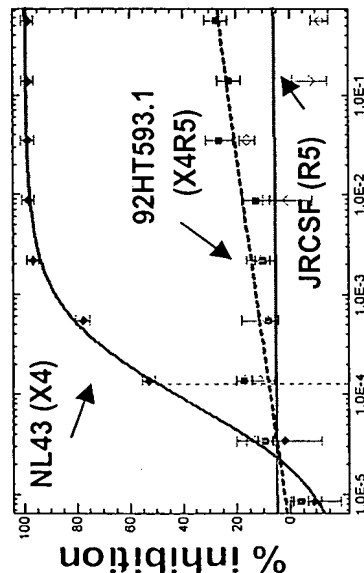


Fig. 8

Fusion Inhibitor Peptides

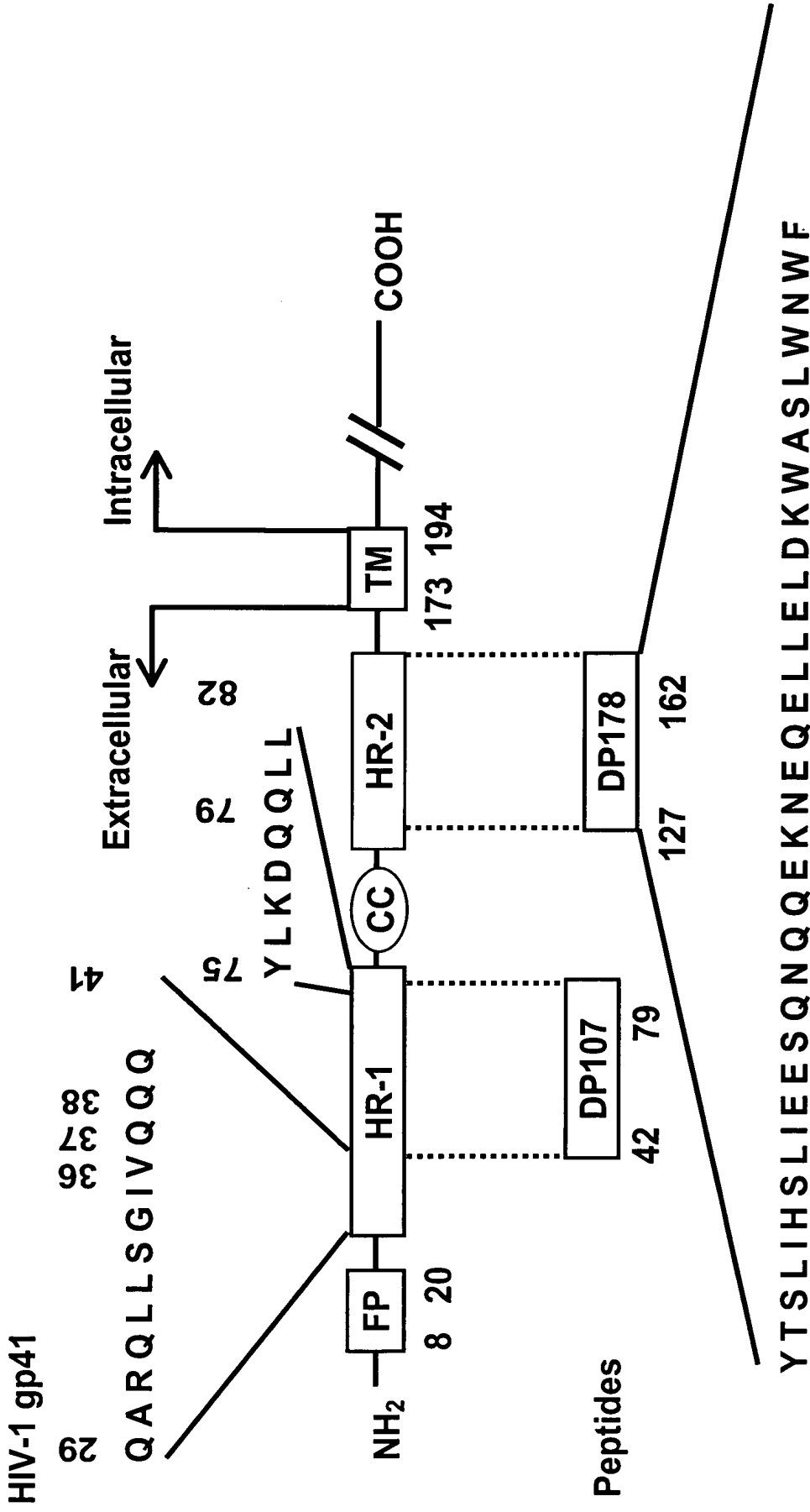


Fig. 9

Rimsky, et al., J. Virol. 72 (2):986-993



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Patient Virus v. Patient Antibody

| Virus Date | Plasma (Antibody) Date | | | | | | | | | |
|------------|------------------------|----------|---------|---------|---------|----------|---------|---------|---------|--|
| | 9/2/99 | 11/29/99 | 2/29/00 | 5/31/00 | 8/30/00 | 11/22/00 | 2/14/01 | 5/30/01 | 9/11/01 | |
| 9/2/99 | 26 | 219 | 675 | 1403 | 2670 | 2089 | 2190 | 2363 | 2411 | |
| 11/29/99 | 29 | 179 | 1024 | 2151 | 3733 | 3152 | 2808 | 2953 | 3086 | |
| 2/29/00 | 27 | 35 | 78 | 358 | 1769 | 1939 | 2247 | 3112 | 4345 | |
| 5/31/00 | 36 | 67 | 82 | 200 | 795 | 1078 | 1371 | 2208 | 3375 | |
| 8/30/00 | 19 | 48 | 36 | 64 | 76 | 166 | 556 | 937 | 1407 | |
| 11/22/00 | 29 | 43 | 64 | 76 | 90 | 119 | 374 | 721 | 1234 | |
| 2/14/01 | 42 | 65 | 61 | 152 | 117 | 134 | 122 | 289 | 526 | |
| 5/30/01 | 41 | 66 | 82 | 84 | 85 | 113 | 78 | 107 | 296 | |
| 9/11/01 | 42 | 62 | 56 | 62 | 85 | 77 | 55 | 61 | 95 | |

Reference Virus

| | | | | | | | | | |
|-------|----|-----|-----|-----|------|-----|------|------|------|
| NL43 | 17 | 138 | 294 | 956 | 1172 | 953 | 1584 | 1868 | 2143 |
| JRCSL | 24 | 37 | 35 | 60 | 87 | 97 | 105 | 152 | 209 |

Fig. 10

